REMARKS

Claims 20-28 are pending in the application and are rejected. Claims 20, 22, 24, 26 and 27 have been amended to better define and distinctly claim what applicants consider to be their invention. New claims 29 and 30 have been added. Reconsideration of the rejection in light of the amendment is respectfully requested for the following reasons:

Claim Rejections Under 35 USC 103

Independent claim 20 continues to be rejected as obvious over Downs in view of Berggren et al. Claim 20 has been amended to particularly point out that the pressure-generating circuit contains a first gas flow of sufficiently high volume to maintain continuous positive pressure in the system, that the respiratory circuit contains a second gas flow of lower volume than the first gas flow, and that the aerosolized medicament is introduced into the second gas flow to avoid dilution of the aerosolized medicament that is delivered to the patient's respiratory system.

Downs teaches the claimed steps of providing a pressure-assisted breathing system having a pressure-generating circuit (14) and a respiratory circuit (16) adapted to be coupled to a patient interface device (20), and engaging the patient interface device with the respiratory system of the patient (18) . Also, as pointed out by the examiner, inhalation by the patient would inherently produce a lower volume gas flow in conduit 16 than in circuit 14. However, Downs lacks the step of introducing an aerosolized medicament into any gas flow of the CPAP disclosed therein, much less in the lower volume gas flow contained in conduit 16. Berggren et al was cited by the examiner as teaching that an aerosolized medicament can be introduced into a gas flow of a CPAP system as a step of a respiratory therapy.

The examiner has failed to identify a valid reason that would have prompted a person of ordinary skill in the relevant field (respiratory therapy) to introduce an aerosolized medicament into a CPAP system as a step in a respiratory therapy because Berggren et al clearly teach that this approach is unsuccessful. In other words, Berggren et al teach away from the claimed invention.

Berggren et al state in the third paragraph of the abstract:

"No beneficial effects of aerosolized surfactant were demonstrated in our trial, contrary to data from animal experiments. This finding probably reflects differences in administration techniques. Our findings do not justify large clinical trials with the same protocol. Further work is needed to optimize delivery of aerosolized surfactant to the neonatal lung in clinical practice."

and in the first full paragraph of page 463:

"…we were unable to demonstrate any beneficial effects of this mode of treatment, neither during the period of nebulization, nor in the outcome statistics."

The cited references establish the scope and contents of the prior art, i.e. there are known methods of respiratory therapy that utilize pressure-assisted breathing systems (e.g. CPAP systems) having a pressure-generating circuit with a first high volume flow to maintain continuous positive pressure in the system and a respiratory circuit adapted to be coupled to a patient interface device which contains a second lower volume flow (e.g. as taught by Downs) and that aerosolized medicament can be introduced into a CPAP system. However, this prior art teaches that the combination is not a successful method of respiratory therapy, at least for babies with RDS, because the amount of medicament retained in the lungs using this method is too low: (see Berggren et al, last paragraph on page 463):

"Our failure to document any beneficial effects of aerosolized surfactant in babies with RDS suggests that, in spite of the precautions taken to enhance delivery, the amount of surfactant retained in the lungs was too low to compensate for the underlying surfactant deficiency and counterbalance the presence of surfactant inhibitors in the airspaces. The same results have been obtained in two other studies using different nebulization set-ups (23,24). Additional efforts should be made to improve currently available techniques for administering aerosolized surfactant to spontaneously breathing newborn babies, and to enhance delivery of the surfactant material to distal airspaces, where it is most needed." (emphasis added)

Berggren et al also teach in the last paragraph of page 463:

"In previous experiments on lung-lavaged rats receiving surfactant aerosol generated by the same technique as in the present trial, < 1% of the aerosolized material could be recovered by bronchoalveolar lavage at the end of the 3-h treatment period (14).

The difference between this prior art and the claims at issue is that, in the claimed method, the aerosolized medicament is introduced into the CPAP system at a location outside the high volume gas flow of the pressure-generating circuit, e.g. into lower gas flow of the

respiratory circuit, to avoid dilution of the aerosolized medicament that is delivered to the patient's respiratory system. For example, in one embodiment of the invention claimed in dependent claim 26, 6-18% of aerosolized surfactant introduced into the system is delivered to the patient, compared to the < 1% obtained using prior art methods reported by Berggren et al.

It is submitted that Berggren et al represent the level of ordinary skill in the art. Since the Downs patent was issued in 1988, the CPAP system taught by Downs was available to Berggren et al . Nonetheless, Berggren et al failed to recognize that the problem of low aerosolized surfactant delivery encountered in the prior art with methods using CPAP systems could be solved by introducing the aerosolized medicament into the lower volume air flow of the respiratory circuit in a CPAP system such as disclosed in Downs many years before, to avoid dilution of the aerosolized medicament that is delivered to the patient. This is strong evidence that the claimed therapy method was beyond the level of ordinary skill in the pertinent art. The long period of time between the first report of the problem by Berggren et al in 2000 and applicants' filing date in 2004 also is evidence that applicants' invention satisfied a long-felt need.

In light of the above analysis, applicants respectively contend that the present claims must be determined to be nonobvious when the *Graham* factors are used to make the obviousness determination.

Claims 21-23, dependent on claim 20, continue to be rejected as obvious over Downs in view of Berggren et al., further in view of Davison. Davison et al. disclose apparatus including a vibrating aperture-type nebulizer that introduces aerosolized medicament into a duct communicating between an air inlet and an outlet port of a non-pressurized dispensing apparatus. Davison et al does not disclose or suggest using a vibrating aperture-type nebulizer in the nonobvious respiratory method of claim 20 to accomplish the step of introducing aerosolized medicament into the respiratory circuit of a pressure-assisted breathing system to avoid dilution of the aerosolized medicament delivered to the patient's respiratory system. Claim 21 is therefore also nonobvious. Claims 22 and 23 are dependent on claim 21 and are therefore nonobvious for the same reasons set forth above in connection with claims 20 and 21.

Claims 25-28 are rejected as obvious over Downs in view of Berggren et al., further in view of Davison. Independent claim 24 also appears to be subject to the same rejection (although the general statement of the rejection on page 6 of the office action excludes claim 24, the examiner applies the rejection to claim 24 in the last paragraph on page 7). Claim 24 has been amended along the same lines as claims 20-23, and is nonobvious for the same reasons discussed in connection with claims 20-23. Claims 25-28 are dependent on claim 24 and are also nonobvious for the same reasons.

New claims 29 and 30 have been added to claim with particularity certain preferred embodiments of the invention.

Claim Objections

Claims 20 and 24 are objected to as not having support in the specification for the recitations "introducing an aerosolized medicament into the lower volume flow of gas" in claim 20, and "entraining the aerosolized surfactant into the second low volume gas flow" in claim 24. The conflicting statement in the specification cited by the examiner (page 5, lines 12 and 13) relates to the CPAP system shown in Fig. 1, which is not within the scope of the claimed invention. Fig. 1 and the accompanying description are included in the specification to compare a method wherein aerosolized medicament 9 is introduced into the high-volume flow of gas 8 in the pressure-generating circuit P with the claimed method shown in Fig. 2. This method is described, for example in paragraph 0025, wherein aerosolized medicament 9 is introduced into lower volume inspiratory flow 18 in respiratory circuit R in accordance with the claims. In light of the foregoing explanation, applicants do not believe that any correction of the specification is required.

CONCLUSION

For the reasons set forth above, applicants contend that all of the claims are in condition for allowance. Accordingly, applicants respectfully request that the examiner reconsider and withdraw the outstanding rejections of the claims, and issue a formal Notice of Allowance at an early date.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

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